REMARKS

Applicants respectfully request a three-months extension of time to April 6, 2007 in which to respond to the official action. The three-months extension fee is charged to the undersigned Attorney's Deposit Account 10-0100. Should additional fees be required or credits are forthcoming, then the additional fees or credits can be charged or credited to the undersigned Attorney's Deposit Account 10-0100.

Applicants have amended the first sentence of the specification to include the claim of priority statement to CU/2002/0292 and PCT/CU2003/000016.

Applicants have amended the specification and claims to correct the informalities in accordance with the Examiner's requirements. No new matter has been added.

The official action of October 6, 2006 suggests the deletion of FIG. 17 as allegedly being redundant to FIG. 15. A close reading of the respective descriptions of FIGS. 15 and 17 reveals a different characterization of the respective FIGS. 15 and 17. As such, there is no redundancy requiring deletion. FIG 17 was therefore not deleted.

Applicants have corrected Figures 2-29 in compliance with 37 CFR 1.121(d) and enclose a set of replacement drawings for all Figures 1-29.

Claim 56 is added.

Claims 1-4, 7-8, 16-19, 22-23, 27-29, 32-33, 39, 42-43 are amended.

Claims 1-56 are presented for further consideration.

Claims 1-55 presently stand rejected under 35 USC § 112, first paragraph as allegedly being of broader scope that the rejection.

Applicant respectfully traverses this rejection.

The Examiner has in effect stated that in the production of antibodies for treatment of leishmaniasis, there is not a sufficient showing. With reference to leishmaniasis, the specification clearly shows protection at prophylactic levels, and the over-simplification to limit the claims only to the production of antibodies does not take in to account the cellular mechanisms involved in protection against leishmaniasis, that are induced by cochlear structures resulting in at least partial protection. Most of the examples are related to the induction of cellular response showing: IL-12 cytokine; nitric oxide and IgG2a subclass production, all suggesting a Th1 (cellular) polarization. In addition, in the specification, applicants refer to the induction of cellular response in several parts. In most of the vaccines, including the TB and HIV reviewed in the two articles suggested by the opponent, the induction of a cellular Th1 immune response is desired. Both articles also pointed out the necessity of an effective adjuvant. The present claims are directed to the novel composition of a cochleate and its intermediaries as potent adjuvants to induce a cellular Th1 immune response. The invention is not only a vaccine composition but also a potent vaccine adjuvant. (See e.g. claim 16 as amended and new claim 56).

While it is generally true that the effectiveness of a vaccine composition is dependent on the microorganism involved, it is also true that to kill most of

the target of the the effector mechanism is often present in the outer membrane. Thus the incorporation of specific protective antigens, especially from the bacterial outer membrane from different microorganisms in the claimed potent adjuvants improves the possibility of a success of any given vaccine. Furthermore, the formulations (whether claimed as a vaccine or a vaccine adjuvant) could effectively be administrated by mucosal route, which is the entry way for most pathogens. The muscosal route is not only readily administerable, but also the only effective way to stimulate secretion of IgA, an antibody related with mucosal protection. (See new claim 56 which further defines this inventive aspect).

The applicant respectfully disagrees with the lack of predictability that the Examiner alleges. Two vaccines are already based in outer membrane vesicles: VA-MENGOC-BC™ (Sierra GVG et al. 1991. NIPH Annals. 14:195-210) and MeNZB™ (Oster P et al. 2005,Vaccine. 23:2191-2196). The former was administered in more than 28 million people in a two dose schedule. The latter was adminstered in New Zealand. The two different vaccines are produced by two different companies. The claimed vaccine induces similar high immune response against a major antigen from the pathogen.

Wang and Xing point out that against TB, the induction of a Th1 pattern is essential and remark the necessity of adjuvant and mucosal vaccination. The lack of an effective adjuvant and particularly a mucosal adjuvant is a principal prior art problem solved by the present invention.

Despite the major challenges surrounding development of an HIV vaccine, Gallo in his article, includes among the oncoming solutions the activation of long lasting production of blocking antibodies, the activation of the innate immunity and the use of potent adjuvant and delivery systems. As described in the present specification, both OMV and cochlear structures activate the innate immune system through the maturation of dendritic cells, production of IL-12 and nitric oxide by dendritic cells and macrophages respectively, as well as a long lasting antibody response. Thus, the present invention opens the possibility to use cochleate structures and OMV as an adjuvant in an HIV vaccine composition. This is manifestly a quantum improvement in the art.

The induction of a particular immune response was referred to in several results and the Figures. in comparison with those induced by VA-MENGOC-BC™ vaccine. The applicants previously demonstrated that this vaccine induces a preferential Th1 pattern of immune response (See Pérez O et al. Infect Immun. 2001, 69(72001):4502-4508). For those reasons, the allegation of the insufficiency of the 'in vitro test' is not sustainable.

The claims specifically claim that the cochlear structure can be obtained from outer membrane vesicles from live microorganism, and a vaccine adjuvant administrable by either mucosal and parenteral routes.

The term 'associated to' that appears in the context of "... molecular pattern associated to pathogens..." in claims 2-4, 27-29, 37-39 and 53 were amended to "...pathogens-associated molecular pattern" which terminology is

prevalent in scientific publications. This terminology refers to the pathogens molecules conserved during evolution which are recognized by pathogen recognition receptors and are the main target in the search for a new effective adjuvant.

The term "... obtained for vesicles found in the outer membrane..." that in other part appeared as "...outer membrane vesicles..." was homogenized and rewritten as the latter form.

Insofar as all the Section 112, first par. have been addressed by this extensive amendment, applicants respectfully request an indication of allowable subject matter. In the event the Examiner believes there are unresolved Section 112, first par. issues, it is respectfully requested that the Examiner telephone the undersigned attorney-of-record; direct dial (914)723-4386.

Respectfully submited,

LACKENBACH SIEGEL, LLP

Marvin Feldman, 25,797

MF:k
Date: April 3, 2007
One Chase Road
Scarsdale, NY 10583
(914) 723-4300